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(12) **United States Patent**  
 Weiss et al.

(10) Patent No.: **US 6,497,872 B1**  
 (45) Date of Patent: **Dec. 24, 2002**

(54) **NEURAL TRANSPLANTATION USING  
 PROLIFERATED MULTIPOTENT NEURAL  
 STEM CELLS AND THEIR PROGENY**

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(\*) Notice: Subject to any disclaimer, the term of this  
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(21) Appl. No.: **08/486,313**

(22) Filed: **Jun. 7, 1995**

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(63) Continuation-in-part of application No. 08/270,412, filed on Jul. 5, 1994, now abandoned, which is a continuation of application No. 07/726,812, filed on Jul. 8, 1991, now abandoned, application No. 08/486,313, which is a continuation-in-part of application No. 08/385,404, filed on Feb. 7, 1995, now abandoned, which is a continuation of application No. 07/961,813, filed on Oct. 16, 1992, now abandoned, which is a continuation-in-part of application No. 07/726,812, application No. 08/486,313, which is a continuation-in-part of application No. 08/359,945, filed on Dec. 20, 1994, now abandoned, which is a continuation of application No. 08/221,655, filed on Apr. 1, 1994, now abandoned, which is a continuation of application No. 07/967,622, filed on Oct. 28, 1992, now abandoned, which is a continuation-in-part of application No. 07/726,812, filed on Jul. 8, 1991, now abandoned, application No. 08/486,313, which is a continuation-in-part of application No. 08/376,062, filed on Jan. 20, 1995, now abandoned, which is a continuation of application No. 08/010,829, filed on Jan. 29, 1993, now abandoned, which is a continuation-in-part of application No. 07/726,812, application No. 08/486,313, which is a continuation-in-part of application No. 08/149,508, filed on Nov. 9, 1993, now abandoned, which is a continuation-in-part of application No. 07/726,812, application No. 08/486,313, which is a continuation-in-part of application No. 08/311,099, filed on Sep. 23, 1994, now abandoned, which is a continuation-in-part of application No. 07/726,812, application No. 08/486,313, which is a continuation-in-part of application No. 08/338,730, filed on Nov. 14, 1994, now abandoned, which is a continuation-in-part of application No. 07/726,812.

(51) Int. Cl. <sup>7</sup> ..... **A01N 63/00; A01N 65/00;  
 A61K 48/00**

(52) U.S. Cl. ..... **424/93.1; 424/93.2; 424/93.21**

(58) Field of Search ..... **424/93.1, 93.2,  
 424/93.21; 514/44**

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(57) **ABSTRACT**

The invention provides methods of transplanting multipotent neural stem cell progeny to a host by obtaining a population of cells derived from mammalian neural tissue containing at least one multipotent CNS multipotent neural stem cell; culturing the neural stem cell in a culture medium containing one or more growth factors which induce multipotent neural stem cell proliferation; inducing proliferation of the multipotent neural stem cell to produce neural stem cell progeny which includes multipotent neural stem cell progeny cells; and transplanting the multipotent neural stem cell progeny to the host. Also provided are methods of transplanting neural stem cell progeny to a host by obtaining an in vitro cell culture containing CNS neural stem cells where one or more cells in the culture (i) proliferates in a culture medium supplemented with one or more mitogens, (ii) retains the capacity for renewed proliferation, and (iii) maintains the multipotential capacity, under suitable culture conditions, to differentiate into neurons, astrocytes, and oligodendrocytes; and transplanting the one or more cells to the host.